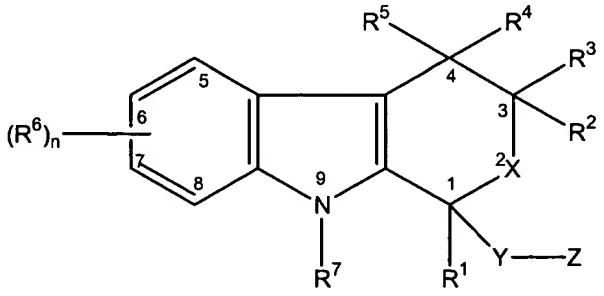
1. (Amended) A compound of formula (I):



(I)

wherein R^1 is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl; each R^6 is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy or [and] thio, Y is [carbonyl,] $(CH_2)_{1-3}$, or $(CH_2)_{1-3}SO_2$ [or $(CH_2)_{1-3}C(O)$,] and Z is (ω-(4-pyridyl)(C_2-C_4alkoxy), (ω-((R^8)(R^9) amino)(C_2-C_4 alkoxy), wherein R^8 and R^9 are each H, (C_1-C_3)alkyl, or together with N, are a 5- or 6-membered heterocyclic ring having [comprising] 1-3 N(R^8), S or nonperoxide O; an amino acid ester of (ω-(HO)(C_2-C_4))alkoxy, N(R^8)CH(R^8)CO_2H, 1'-D-glucuronyloxy, [; or Y-Z is $(CH_2)_{1-3}R^8$; wherein R^8 is] OH, (C_2-C_4)acyloxy, SO_3H, PO_4H_2, N(NO)(OH), SO_2NH_2, PO(OH)(NH_2), $OCH_2CH_2N(CH_3)_3^+$, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl;

provided that when n is 1, R^6 is hydrogen, and R^1 is methyl, then-Y-Z is not $-CH_2CH_2$-OH, $-CH_2$-OH, $-CH_2CH_2$-$OC(O)CH_3$, or $-CH_2$-$OC(O)CH_3$; and provided that when n is 1, R^6 is 8-ethyl, and R^1 is ethyl, then -Y-Z is not $-CH_2CH_2$-OH, or $-CH_2CH_2$-$OC(O)CH_3$;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 wherein Z is the L-valine or L-glycine ester of 2-hydroxyethoxy.

3. The compound of claim 1 wherein Z is N-morpholinoethoxy.

4. The compound of claim 1 wherein each R^8 is H, CH_3 or i-Pr.

5. The compound of claim 1 wherein Z is $OCH_2CH_2N(CH_3)_3^+$.

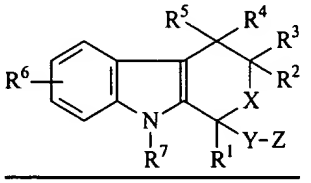
6. A composition comprising the compound of claim 1 in combination with a pharmaceutically acceptable carrier.

7. The composition of claim 6 which is a tablet, granule or capsule.

8. The composition of claim 6 wherein the carrier is an aqueous vehicle.

9. The composition of claim 8 which is an aqueous solution.

10. (Amended) A method of inhibiting the viability of cancer cells in a mammal comprising administering an effective amount of [the] a compound of [claim 1] formula (I):



(I)

wherein R^1 is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl; each R^6 is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl, $(CH_2)_{1-3}$, $(CH_2)_{1-3}SO_2$ or $(CH_2)_{1-3}C(O)$, and Z is (ω-(4-pyridyl)(C_2-C_4alkoxy), (ω-((R^8)(R^9) amino)(C_2-C_4 alkoxy),

wherein R^8 and R^9 are each H, $(C_1\text{-}C_3)$alkyl or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 $N(R^8)$, S or nonperoxide O; an amino acid ester of $(\omega\text{-}(HO)(C_2\text{-}C_4))$alkoxy, $N(R^8)CH(R^8)CO_2H$, 1'-D-glucuronyloxy, OH, $(C_2\text{-}C_4)$acyloxy, SO_3H, PO_4H_2, $N(NO)(OH)$, SO_2NH_2, $PO(OH)(NH_2)$, $OCH_2CH_2N(CH_3)_3^+$, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with cancer.

11. A method of inhibiting cancer comprising administering an effective amount of the composition of claim 6 to a mammal afflicted with cancer.

12. The method of claim 10 or 11 wherein the cancer is prostate cancer.

13. The method of claim 10 or 11 wherein the cancer is multiple myeloma.

14. The method of claim 10 or 11 wherein the cancer is chronic lymphocytic leukemia.

15. The method of claim 11 wherein the composition is administered orally.

16. The method of claim 15 wherein an enterically coated dosage form is administered.

17. The method of claim 11 wherein the composition is administered parenterally.

18. The method of claim 11 wherein the composition is administered in combination with a chemotherapeutic agent.

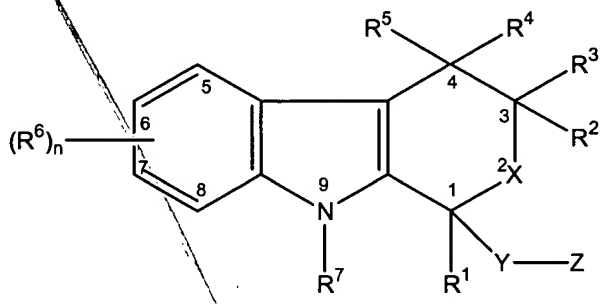
19. The method of claim 12 wherein the composition is administered in combination with a chemotherapeutic agent.

Clean Version of Pending Claims

INDOLE COMPOUNDS USEFUL FOR THE TREATMENT OF CANCER
Applicant: Dennis A. Carson et al.
Serial No.: 09/634,207

a3

1. (Amended) A compound of formula (I):



(I)

wherein R^1 is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl, benzyl or 2-thienyl, R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl; each R^6 is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower-alkanoyloxy, nitro or halo, n is 1-3, R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is $(CH_2)_{1-3}$, or $(CH_2)_{1-3}SO_2$ and Z is (ω-(4-pyridyl)(C_2-C_4alkoxy), (ω-((R^8)(R^9) amino)(C_2-C_4 alkoxy), wherein R^8 and R^9 are each H, (C_1-C_3)alkyl, or together with N, are a 5- or 6-membered heterocyclic ring having 1-3 N(R^8), S or nonperoxide O; an amino acid ester of (ω-(HO)(C_2-C_4))alkoxy, N(R^8)CH(R^8)CO_2H, 1'-D-glucuronyloxy, OH, (C_2-C_4)acyloxy, SO_3H, PO_4H_2, N(NO)(OH), SO_2NH_2, PO(OH)(NH_2), $OCH_2CH_2N(CH_3)_3^+$, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl;

provided that when n is 1, R^6 is hydrogen, and R^1 is methyl, then-Y-Z is not -CH_2CH_2-OH, -CH_2-OH, -CH_2CH_2-OC(O)CH_3, or -CH_2-OC(O)CH_3; and provided that when n is 1, R^6 is 8-ethyl, and R^1 is ethyl, then -Y-Z is not -CH_2CH_2-OH, or -CH_2CH_2-OC(O)CH_3;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 wherein Z is the L-valine or L-glycine ester of 2-hydroxyethoxy.

3. The compound of claim 1 wherein Z is N-morpholinoethoxy.

4. The compound of claim 1 wherein each R^8 is H, CH_3 or i-Pr.

5. The compound of claim 1 wherein Z is $OCH_2CH_2N(CH_3)_3^+$.

6. A composition comprising the compound of claim 1 in combination with a pharmaceutically acceptable carrier.

7. The composition of claim 6 which is a tablet, granule or capsule.

8. The composition of claim 6 wherein the carrier is an aqueous vehicle.

9. The composition of claim 8 which is an aqueous solution.

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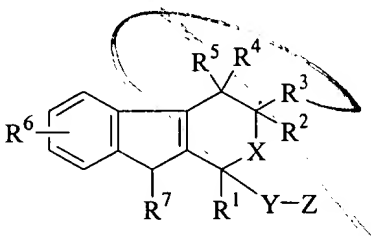
10. (Amended) A method of inhibiting the viability of cancer cells in a mammal comprising administering an effective amount of a compound of formula (I):



(I)

wherein R^1 is lower alkyl, lower alkenyl, (hydroxy)lower alkyl, lower alkynyl, phenyl,

benzyl or 2-thienyl, R^2, R^3, R^4 and R^5 are the same or different and are each hydrogen or lower alkyl; each R^6 is individually hydrogen, lower alkyl, hydroxy, (hydroxy)lower alkyl, lower alkoxy, benzyloxy, lower alkanoyloxy, nitro or halo, n is 1-3, R^7 is hydrogen, lower alkyl or lower alkenyl, X is oxy or thio, Y is carbonyl, $(CH_2)_{1-3}$, $(CH_2)_{1-3}SO_2$ or $(CH_2)_{1-3}C(O)$, and Z is (ω-(4-pyridyl)(C_2-C_4alkoxy), (ω-((R^8)(R^9) amino)(C_2-C_4 alkoxy), wherein R^8 and R^9 are each H, (C_1-C_3)alkyl or, together with N, are a 5- or 6-membered heterocyclic ring having 1-3 N(R^8), S or nonperoxide O; an amino acid ester of (ω-(HO)(C_2-C_4))alkoxy, N(R^8)CH(R^8)CO_2H, 1'-D-glucuronyloxy, OH, (C_2-C_4)acyloxy, SO_3H, PO_4H_2, N(NO)(OH), SO_2NH_2, PO(OH)(NH_2), $OCH_2CH_2N(CH_3)_3^+$, amino, lower alkylamino, di(lower alkyl)amino, phenylamino, or tetrazolyl; or a pharmaceutically acceptable salt thereof; to a mammal afflicted with cancer.

11. A method of inhibiting cancer comprising administering an effective amount of the composition of claim 6 to a mammal afflicted with cancer.

12. The method of claim 10 or 11 wherein the cancer is prostate cancer.

13. The method of claim 10 or 11 wherein the cancer is multiple myeloma.

14. The method of claim 10 or 11 wherein the cancer is chronic lymphocytic leukemia.

15. The method of claim 11 wherein the composition is administered orally.

16. The method of claim 15 wherein an enterically coated dosage form is administered.

17. The method of claim 11 wherein the composition is administered parenterally.

18. The method of claim 11 wherein the composition is administered in combination with a chemotherapeutic agent.

D1 cont

19. The method of claim 12 wherein the composition is administered in combination with a chemotherapeutic agent.

D1 cont

20. (Amended) The method of claim 18 wherein the chemotherapeutic agent is mitoxantrone, prednisone, estramustine, melphalan, vinblastine or a combination thereof.

Q5

21. (Amended) The method of claim 19 wherein the chemotherapeutic agent is an anti-androgen.

D1 cont

22. The method of claim 21 wherein the anti-androgen is bicafutamide, nilutamide, flutamide, cycloproterone acetate or a combination thereof.

23. The method of claim 21 wherein the anti-androgen is leuprolide acetate, goserelin acetate or a combination thereof.

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